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# Antimicrobial therapy in older adults: profile of use and evaluation of the quality of prescription

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## Abstract

**Objectives:** To analyze the point prevalence of antimicrobial agent use by older adults and to determine the quality of use in a teaching hospital. A pharmacoepidemiological, observational study. **Methods:** Retrospective collection of clinical, microbiological and pharmacotherapeutic data in medical records. Inclusion criteria: age ≥ 60 years old, in use of one or more antimicrobial agents. The resistant microorganisms classified as priority pathogens by the World Health Organization (WHO) were identified. The quality of antimicrobial agent use according to quality indicators described by Van den Bosch *et al*. (2015) was determined. A descriptive statistical analysis was performed. **Results:** Of the 130 hospitalized older adult individuals, 40.8% were using one or more antimicrobials agents on the day of point prevalence. Among the 50 resistant microorganisms identified in the cultures, 54.0% corresponded to pathogens of critical priority. Antibiotic glycopeptides (14.9%) and penicillins associated with beta-lactamase inhibitors (13.8%) were the most prescribed classes of antimicrobial agents. The Quality Indicators (QIs) of antimicrobial therapy demonstrated more frequent inadequacy regarding therapeutic monitoring, sequential therapy and blood culture request. **Conclusions:** The prevalence of antimicrobial agent use in older adults was high. Empirical therapy is often developed in line with that advocated by the Infection Control Commission. The high isolation of critical pathogens according to the WHO, evidences the importance of actions to ensure the rational use of drugs in the institution. The QIs demonstrated the need to implement guidelines for systematizing therapeutic antimicrobial agent monitoring in the institution and educational action on the process of requesting blood cultures.

**Keywords:** anti-infective agents, aged, antimicrobial stewardship, drug resistance, microbial, quality indicators, health care, observational study.

# Terapia antimicrobiana em idosos: perfil de uso e avaliação da qualidade da prescrição

## Resumo

**Objetivos:** Analisar a prevalência pontual de utilização de antimicrobianos por idosos e determinar a qualidade do uso em um hospital de ensino. **Métodos:** Estudo farmacoepidemiológico, observacional. Coleta retrospectiva de dados clínicos, microbiológicos e farmacoterapêuticos em prontuário. Critérios de inclusão: idade ≥ 60 anos, em uso de um ou mais antimicrobianos. Identificou-se os microorganismos resistentes classificados como agentes patogênicos prioritários pela Organização Mundial da Saúde (OMS). Determinou-se a qualidade do uso de antimicrobianos segundo indicadores de qualidade de Van den Bosch *et al*. (2015). Realizou-se análise estatística descritiva. **Resultados:** Dos 130 idosos internados, 40,8% estavam em uso de um ou mais antimicrobianos no dia da prevalência pontual. Entre os 50 microorganismos resistentes identificados nas culturas, 54,0% correspondiam a agentes patogênicos de prioridade crítica. Glicopeptídeos antibacterianos (14,9%) e penicilinas associadas a inibidores de beta-lactamase (13,8%) foram as classes de antimicrobianos mais prescritas. Os indicadores de qualidade (IQs) de terapia antimicrobiana demonstraram inadequação mais frequente em relação à monitorização terapêutica, terapia sequencial e solicitação de hemocultura. **Conclusões:** A prevalência do uso de antimicrobianos nos idosos foi elevada. A terapia empírica é frequentemente desenvolvida em consonância com o preconizado pela comissão de controle de infecções. O isolamento elevado de agentes patogênicos críticos segundo OMS, evidenciam a importância de ações para garantir o uso racional de medicamentos na instituição. Os IQs demonstraram a necessidade de implementar diretrizes para sistematizar a monitorização terapêutica de antimicrobianos na instituição e ação educativa sobre o processo de solicitação de hemoculturas.

**Palavras-chave:** anti-infecciosos, idoso, gestão de antimicrobianos, resistência microbiana a medicamentos, indicador de qualidade em assistência à saúde, estudo observacional.

## Introduction

Microbial resistance is a biological and natural phenomenon, involving complex mechanisms, resulting mainly from the inappropriate use of antimicrobial agent agents[1,2]. There is an increasing number of microorganisms resistant to antimicrobials agents used in clinical practice, both on an outpatient and hospital level, constituting a public health problem. The dimension of the problem becomes even more worrying, as there is evidence of low development rate of new antimicrobial agents[3].

There are few therapeutic options for treating infections by resistant microorganisms[3]. Thus, strategies that contribute to the appropriate use of antimicrobials agents must be implemented in health services.

A growing body of national and international evidence shows that hospital programs aimed at improving the use of antimicrobial agents, commonly referred to as Antibiotic Stewardship Programs (ASPs), can optimize the treatment of infections and reduce the adverse events associated with their use[4,5]. In Brazil, the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária,* ANVISA) proposed the following name: *Antimicrobial Agent Use Management Program*[6]. These programs guarantee the quality of care and improve patient safety.

With senescence, there is an increase in the consumption of drugs and morphophysiological changes that can result in a decrease in the ability to perform an effective immune response, which makes infections in the older adult more severe and complicated[2]. In addition, the older adult may have pharmacokinetic and pharmacodynamic changes, increasing the risk of developing adverse reactions to the drug[7].

Monitoring of the appropriate use of antimicrobial agents can be performed using quality indicators that measure the adequacy of the use of antimicrobials agents in the treatment of infections in hospitalized patients[8]. The available Quality Indicators (QIs) have been systematically extracted from international guidelines and from the specialized literature[8-10].

Considering the impact of the inappropriate use of antimicrobial agents, it is important to develop studies that aim to know the prevalence of their use, especially by the older adult, and the main factors that can contribute to the occurrence of microbial resistance.

The present study aims to describe the profile of antimicrobial agent use by the older adult and to determine the quality of the use of antimicrobials agents in a teaching hospital in Belo Horizonte.

## Methods

A pharmacoepidemiological, observational, retrospective, descriptive study, carried out in a public teaching hospital with 320 beds, inserted in the Unified Health System (*Sistema Único de Saúde*, SUS). It is a referral hospital, integrated to the urgency and emergency care system in the metropolitan region of Belo Horizonte, with maternal, child and surgical care lines.

The prescription of antimicrobials agents in the hospital is computerized with a 24-hour validity. The distribution system for antimicrobials agents and other drugs is individualized, direct and separated by schedule with delivery every 12 hours. The antimicrobial agent audit is global, prospective and performed by the Hospital Infection Control Commission. For strategic antimicrobials agents (high cost and wide spectrum) it is necessary to fill out a form with justification for use, which will be evaluated by the Pharmacy.

The criteria for inclusion in the study were: being older adult, using at least one antimicrobial agent for systemic use (belonging to groups J01 to J05 of the Anatomical Therapeutic Chemical classification) on September 20th, 2017[11]. The definition of older adult for developing countries (60 years or older) was adopted in this investigation[12]. Patients under the age of 60 and those admitted to the emergency room and maternity ward, regardless of age, were excluded.

The information related to the study variables was collected by consulting the electronic medical record and documented in a data collection instrument developed for the purposes of the research. The point prevalence of the use of antimicrobials agents (PPUAM) was determined for the patients who met the inclusion criteria. The PPUAM was calculated by dividing the number of older adult people using antimicrobials agents by the number of older adult admitted to inpatient units.

The other study variables include sociodemographic characteristics (gender, age), related to health services (hospitalization clinic, length of stay in days, ICU stay, death) and clinical (diagnosis of admission, comorbidities, infection on admission, infection site on admission, hospital infection, invasive procedures, microbiological testing).

The diagnoses on hospital admission were identified and grouped according to the tenth edition International Classification of Diseases (ICD10). The microorganisms identified in the microbiological tests were classified according to the list of priority pathogens according to the World Health Organization (WHO). This list was developed considering the threat to human health and to guide research and development of new antimicrobial agents, considering the increase in resistance[13].

The quality of the rational use of antimicrobials agents in the investigated hospital was evaluated using the QIs described by Van den Bosch *et al*. (2015). These indicators were developed using the Delphi Method modified by RAND. Eleven generic QIs were structured to assess the appropriate use of antimicrobials agents in hospitalized patients, excluding those admitted to the intensive care unit. Of these, nine are process indicators, measuring the process around the appropriate use of antimicrobials agents at the patient level: 1. Before starting systemic antibiotic therapy, at least two sets of blood cultures should be taken; 2. When starting systemic antibiotic therapy, specimens for culture from suspected sites of infection should be taken as soon as possible, preferably before antibiotics are started. (cultures should be obtained no later than 24 hours after the start of antibiotics); 3. Empirical systemic antibiotic therapy was prescribed according to local guidance; 4 Empirical antibiotic therapy should be changed to pathogen-directed therapy if culture results become available; 5. Dose and dosing interval of systemic antibiotic therapy should be adapted to renal function; 6. Systemic antibiotic therapy should be switched from i.v. to oral antibiotic therapy within 48 -72 hr on the basis of the clinical condition and when oral treatment is adequate; 7. An antibiotic plan should be documented in the case notes at the start of systemic antibiotic therapy; 8. Therapeutic drug monitoring should be performed when the therapy duration is >3 days for aminoglycosides and >5 days for vancomycin; 9. Empirical antibiotic therapy for presumed bacterial infection should be discontinued based on the lack of clinical and/or microbiological evidence of infection. The maximum duration of empirical systemic antibiotic treatment should be 7 days.

The indicator regarding the dose adjustment according to renal function (QI- 5) was not measured in the present study.

QIs 10 and 11 are structure indicators and measure the requirements for appropriate use of antimicrobials agents at the

hospital level: 10. A current local guideline on the use of antibiotics must be present at the hospital and an update must be made every three years; 11. Local guidelines for the use of antibiotics should correspond to national guidelines, but should be based on the institution's standards for resistant microorganisms.

The calculation of the indicators was performed using the absolute frequency of patients whose antibiotic therapy had the characteristics described in the indicator as the numerator and the number of patients using antimicrobials agents as the denominator. For indicators referring to targeted therapy, sequential antimicrobial therapy and conducting therapeutic monitoring, the denominators include patients who were using antimicrobials agents in conditions that provided measurement.

The feasibility of indicating sequential oral therapy was performed considering the following parameters: 1. Availability of an antimicrobial agent suitable for oral administration; 2. Improvement of signs and symptoms of infection based on objective clinical parameters; 3. Afebrile for at least 8 hours; 4. Regularization of the leukocyte count to normal values; 5. Ability to use the oral route; 6. Functional gastrointestinal tract (absence of nausea, vomiting, malabsorption syndrome, motility disorder and short bowel syndrome); 7. Presence of two or more parameters that determine the indication of the parenteral route, taking into account the patient's clinical situation (temperature > 38ºC; tachycardia > 90 beats per minute; respiratory rate > 20 inspirations per minute; leukocyte global < 4,000 or > 12,000/ $mm^3$; sepsis of undetermined origin; systolic pressure ≤ 90mmHg; chills or tremors with hepatic, renal or mental confusion)[14].

The collected data were recorded in a Microsoft Excel® spreadsheet. For the descriptive analysis of the data, absolute and relative frequencies were performed for categorical variables and measures of central tendency (median) and measures of dispersion (interquartile range - IQR) for quantitative variables. The normality assessment was performed according to the Shapiro Wilk test. Statistical analyses were performed using SPSS software, version 25.0.

This study was approved by the Research Ethics Committee of the Federal University of Minas Gerais *(Comitê de Ética em Pesquisa da Universidade Federal de Minas Gerais*, COEP-UFMG), under CAAE 89454218.0.0000.5149, with exemption from the Free and Informed Consent Form.

## Results

On the day of the point prevalence study, 320 individuals were admitted to the hospital wards. One hundred and thirty were older adult and 53 of them were using one or more antimicrobial agents; therefore, the PPUAM among the older adult was 40.8%.

Table 1 shows the sociodemographic characteristics, related to care and to the clinics. The median age of the older adult who received antimicrobial agent therapy was 71 years old and IQR equal to 12; 67.9% were male. Most of the individuals had two or more chronic diseases, the most reported being systemic arterial hypertension (69.8%), followed by diabetes mellitus (50.9%).

The main diagnoses observed at hospital admission were diseases of the circulatory system (19; 35.8%), injuries, poisoning and some other consequences of external causes (6; 11.3%), diseases of the respiratory system (5; 9.4%) and endocrine, nutritional and metabolic diseases (5; 9.4%). The median hospital stay was 27 days and the IQR was 8, with 31 older adult people hospitalized under general care on the day of the point prevalence analysis. 22 individuals were admitted to the Intensive Care Unit (ICU), where 40.9% of the cases were related to infection. There was a death outcome in 30.2% of the 53 older adult people using antimicrobials agents on the day of point prevalence.

**Table 1.** Characteristics of hospitalized older adult people who used antimicrobials agents on the day of the point of prevalence (n = 53), Belo Horizonte, 2017.

| Variables | Values |
|---|---|
| **SOCIODEMOGRAPHIC** | |
| **Age in years old [median (interquartile amplitude)]** | 71 (69-74) |
| **Gender [male n (%)]** | 36 (67.9) |
| **RELATED TO CARE** | |
| **Days of hospitalization [median (interquartile amplitude)]** | 27 (24-42) |
| **Hospitalization clinic - n (%)** | |
| General surgery | 15 (28.3) |
| General clinic | 31 (58.5) |
| Neurology | 2 (3.8) |
| Orthopedics/Traumatology | 5 (9.4) |
| **ICU admission - n (%)** | 22 (41.5) |
| **ICU admission due to infection - n (%)** | 9 (40.9) |
| **Death - n (%)** | 16 (30.2) |
| **CLÍNICAL** | |
| **Comorbidities - n (%)** | |
| Cerebral Vascular Accident | 11 (20.8) |
| Diabetes Mellitus | 27 (50.9) |
| Chronic Obstructive Pulmonary Disease | 12 (22.6) |
| Chronic Kidney Disease | 11 (20.8) |
| Peripheral Vascular Disease | 7 (13.2) |
| Atrial Fibrillation | 8 (15.1) |
| Systemic Arterial Hypertension | 37 (69.8) |
| Heart Failure | 12 (22.6) |
| Neoplasm | 7 (13.2) |
| **Infection at admission - n (%)** | 32 (60.4) |
| **Infection site at admission - n (%)** | |
| Respiratory tract | 7 (21.9) |
| Urinary tract | 5 (15.6) |
| Skin and soft tissues | 19 (59.4) |
| Surgical site | 1 (3.1) |
| **Hospital infection n (%)** | 28 (52.8) |

The presence of infection at admission was reported in the medical records of 60.4% of the patients. Twenty-eight (52.8%) patients acquired infection in the hospital setting. 113 invasive procedures were identified among the older adult included in the study, most of them peripheral venous access (43.4%), followed by delayed bladder catheter (18.6%), implantation of central vascular access (15, 0%), enteric tube (14.1%), tracheostomy (5.3%), vesical relief tube (2.7%), and ostomy (0.9%).

For microbiological propaedeutics, 105 cultures were performed with the following distribution: urine culture (31; 58.5%), blood culture (25; 47.2%), deep tissue (16; 30.2%), tracheal aspirate (11; 20.8%), catheter tip (7; 13.2%), alcohol-resistant acid bacillus (ACRB) (5; 9.4%) and other cultures (10; 18.9%). There were 70 microorganisms identified, 50 of which were on the WHO list. Most were *Enterobacteriaceae,* resistant to carbapenems and producing ESBL and *Staphylococcus aureus* resistant to methicillin, with intermediate sensitivity and resistance to vancomycin, classified as priority 1 and priority 2, respectively, according to the WHO criteria (Table 2).

**Table 2.** Microorganisms identified in the microbiological propaedeutics according to the WHO list of pathogens that pose a threat to human health (n = 50), Belo Horizonte, 2017.

| Variables | n | (%) |
|---|---|---|
| **Priority 1: CRITICAL** | | |
| *Acinetobacter baumannii,* resistant to carbapenems | 5 | 10.0 |
| *Pseudomonas aeruginosa*, resistant to carbapenems | 4 | 8.0 |
| *Enterobacteriaceae,* carbapenem-resistant, ESBL-producing* | 27 | 54.0 |
| **Priority 2: HIGH** | | |
| *Enterococcus faecium*, resistant to vancomycin | 2 | 4.0 |
| *Staphylococcus aureus*, resistant to methicillin, with intermediate sensitivity and resistance to vancomycin | 12 | 24.0 |
| *Helicobacter pylori*, resistant to clarithromycin | 0 | 0 |
| *Campylobacter spp*. resistant to fluoroquinolones | 0 | 0 |
| *Salmonella spp.*, resistant to fluoroquinolones | 0 | 0 |
| *Neisseria gonorrhoeae,* resistant to cephalosporin, resistant to fluoroquinolones | 0 | 0 |
| **Priority 3: MEDIUM** | 0 | 0 |
| *Streptococcus pneumoniae*, without sensitivity to penicillin | 0 | 0 |
| *Haemophilus influenzae*, ampicillin resistant | 0 | 0 |
| *Shigella spp*., resistant to fluoroquinolones | 0 | 0 |

*Enterobacteriaceae* include: *Klebsiella pneumoniae, Escherichia coli, Enterobacter spp., Serratia spp., Proteus spp., Providencia spp,* and *Morganella spp*.

**Table 3.** Description of the antimicrobials agents for systemic use used by the older adult included in the study according to the Anatomical Therapeutic Chemical (ATC) classification (n = 53), Belo Horizonte, 2017.

| ATC Code | Group and subgroup of the medications | n | % |
|---|---|---|---|
| J01 | Antibacterials for systemic use | | |
| J01A | Tetracyclines | | |
| J01AA | Tetracyclines: tigecycline | 1 | 1.1 |
| J01C | Penicillins, beta-lactam antibacterials | | |
| J01CF | Beta-lactamase resistant penicillins: oxacilin | 2 | 2.3 |
| J01CR | Penicillins associated with beta-lactamase inhibitors: piperacillin+tazobactam | 12 | 13.8 |
| J01D | Other beta-lactam antibacterials | | |
| J01DB | First generation cephalosporins: cefazolin, cephalexin | 3 | 3.5 |
| J01DD | Third generation cephalosporins: ceftazidime, ceftriaxone | 5 | 5.7 |
| J01DE | Fourth generation cephalosporins: cefepime | 9 | 10.4 |
| J01DH | Carbapenems: meropenem | 10 | 11.5 |
| J01E | Sulphonamides and trimethoprim | | |
| J01F | Macrolides, Lincosamides and Streptogramins | | |
| J01FA | Macrolids: azithromycin, clarithromycin | 2 | 2.3 |
| J01G | Aminoglycosides: amikacin and gentamicin | | |
| J01GB | Other aminoglycosides | 3 | 3.5 |
| J01M | Antibacterial quinolones: ciprofloxacin, levofloxacin | | |
| J01MA | Fluoroquinolones | 3 | 3.5 |
| J01X | Other antibacterials | | |
| J01XA | Antibacterial glycopeptide: vancomycin, teicoplanin | 13 | 14.9 |
| J01XB | Polymyxins: Polymyxin B | 6 | 6.9 |
| J01XD | Imidazole derivatives: metronidazole | 8 | 9.2 |
| J01XX | Other antibacterials: daptomycin | 2 | 2.3 |
| J02 | Antimycotics for systemic use | | |
| J02A | Antimycotic for systemic use | | |
| J02AC | Triazole derivatives: fluconazole | 5 | 5.7 |
| J04 | Antimycobacterials | | |
| J04A | Drugs for the treatment of tuberculosis | | |
| J04AM | Drug combinations for treating tuberculosis: rifampicin + isoniazid + pyrazinamide + ethambutol | 1 | 1.1 |
| J05 | Antiviral drugs for systemic use | | |
| J05A | Direct acting antivirals | | |
| J05AB | Nucleoside and nucleotide, except reverse transcriptase inhibitors: acyclovir | 2 | 2.3 |
| | Total | 87 | 100.0 |

On the day of PPUAM determination, it was observed that the main classes of antimicrobials agents prescribed were antibacterial glycopeptide (14.9%), penicillins associated with beta-lactamase inhibitors (13.8%), and carbapenems (11.5%). The median use of antimicrobials agents on the day of PPUAM was 2 (IRQ = 1).

The indicators with the lowest adequacy rate were those related to therapeutic monitoring (5.9%), and sequential oral therapy (36.7%), followed by the request for blood culture (47.2%). Of the 17 older adult people who used vancomycin during hospitalization, plasma monitoring was performed in only one (5.9%) individual. Plasma monitoring was not requested for any of the seven older adult individuals who used aminoglycosides. The values of the other indicators were higher than 69.8% (Table 4).

**Table 4.** Evaluation of the Quality Indicators (n = 53), 2017, Belo Horizonte, 2017.

| | Variables | n | % |
|---|---|---|---|
| 1. | Before starting the systemic antibiotic therapy, at least two blood cultures were requested. | 25 | 47.2 |
| 2. | When initiating the systemic antibiotic therapy, samples of sites suspected of infection for the culture were obtained as soon as possible, preferably before antibiotics were started (cultures should be obtained for up to a maximum of 24 hours after antibiotics started). | 37 | 69.8 |
| 3. | The empirical systemic antibiotic therapy was prescribed according to local guidance. | 40 | 75.5 |
| 4. | The empirical antibiotics were changed to targeted therapy when culture results were available - n (%)* | 33 | 97.1 |
| 5. | The systemic antibiotic therapy was switched to oral administration within 48-72 hours based on the clinical condition and when oral treatment was appropriate - n (%)* | 11 | 36.7 |
| 6. | The planning of the antibiotic therapy was documented at the beginning of the treatment with the systemic antibiotic - n(%) | 53 | 100.0 |
| 7. | Plasma therapeutic monitoring was performed when the duration of the treatment was greater than three days for aminoglycosides and greater than five days for vancomycin - n (%)* | 1 | 5.9 |
| 8. | The empirical antibiotic therapy was discontinued in case of lack of clinical and/or microbiological evidence. The maximum duration of the treatment with empirical systemic antibiotics did not exceed 7 days - n (%)* | 49 | 92.5 |

* For the targeted therapy indicators (n=34), sequential oral therapy (n=30) and therapeutic monitoring (n=17), the denominators include patients for whom the measurement is relevant.

## Discussion

The point prevalence study of the use of antimicrobials agents is a useful surveillance method to obtain information on hospital epidemiology and has been widely used in several countries[15,16]. The present study is one of the first to investigate the use of antimicrobial agent drugs among older adult patients hospitalized in Brazil and showed a high prevalence in line with national and international studies.

High prevalence of antimicrobial agent use, varying from 48.6% in the south to 60.4% in the northeast, was detected in the study of punctual prevalence of antimicrobials agents carried out in 18 Brazilian hospitals using the methodology of the international project called Global Point Prevalence Survey of antimicrobial agent Consumption and Resistance (GLOBAL-PPS) which aims to raise awareness about multidrug resistance and contribute to the development of actions to improve the quality of antimicrobial agent prescriptions[17]. The prevalence in national studies is higher than that detected in European hospitals using the GLOBAL-PPS methodology, where the rate was 30 to 40%[17]. On the other hand, a Latin American study that included three tertiary hospitals in Brazil found a prevalence of around 30% and lower than that of hospitals in other countries[18]. It is worth mentioning that the three hospitals were in the south and southeast regions of Brazil, which may explain the lower prevalence. The use of antimicrobials agents is mainly determined by the health care profile of the hospital and by the educational actions for infection control developed in the institutions, factors that may explain the variation in prevalence found in different studies.

PPUAM studies in Brazilian and international hospitals do not present stratified prevalence data for the older adult. In this sense, the comparison of our data with other studies should be performed with caution. However, it is worth mentioning that being ≥ 70 years old was a risk factor for infection related to health care in Brazilian hospitals[18]. As a result, there is a high use of antimicrobials agents in this age group during hospitalization, as evidenced in the present study.

The median number of antimicrobial agents was two, a finding that is also in line with the multicentric study of PPUAM conducted in Brazil, which showed a high proportion of patients using two or more antimicrobial agents[17]. The use of multiple antimicrobials agents must be carried out with solid scientific evidence, as inappropriate use can contribute to multi-drug resistance and the occurrence of adverse events[5,6,19]. In the hospital setting, antimicrobials agents are often prescribed and used incorrectly, especially in relation to dose adjustment and dosage in the older adult, which can result in damage to the patient[19]. Therefore, greater multi-professional monitoring and follow-up is necessary for the older adult so that the risk in the use of medications is not greater than the possible clinical benefits.

The investigated hospital is a reference in the municipality for the treatment of peripheral vascular diseases, which explains the predominance of skin and soft tissue infections at hospital admission. Regarding the treatment of chronic diabetic ulcer infections, coverage for anaerobic microorganisms may be necessary[20], which justifies the use of metronidazole observed in the present study.

Among the registered infections, 52.8% were acquired at the hospital. It is likely that they are mainly related to invasive procedures performed during hospitalization. The increased use of invasive procedures and devices and inadequate infection control practices are important transmission routes healthcare-related infections in hospitals and contribute to antimicrobial agent resistance[1]. Furthermore, the concern with infection leads to the early use of broad-spectrum empirical antimicrobial agent agents, which contributes to the development of multi-resistant microorganisms[1,16].

The pathogens identified in the study are classified as critical and high priority for the development and research of more effective antibiotic treatments[13]. The relevance of cultures is highlighted, as they support the rational use of antimicrobial agents, contributing to the reduction of microbial resistance. The spread of microbial resistance to antibiotics results in increased morbidity and mortality, length of hospital stay and higher medical costs[1]. These findings are worrying, since the main risk is the emergence of bacterial resistance, and the impact on the ecology of the microbiota is not only individual, but also collective. Therefore, considering these dimensions, it is a public health problem.

The presence of penicillins associated with beta-lactamase inhibitors, third-generation cephalosporins, carbapenems and glycopeptides among the most used drugs, as well as the high frequency of drugs in the J01 group, are in line with the national and Latin American study of PPUAM. This antimicrobial agent profile reflects the increased prevalence of microorganisms such as methicillin-resistant *Staphylococcus aureus* (MRSA)[21] demanding the use of vancomycin and teicoplanin and also the increase in resistance to antimicrobial agents, mainly by gram-negative bacteria, justifying the prescription of meropenem and piperacillin + tazobactam[17].

In addition to knowing the profile of antimicrobial agents, it is essential to verify whether the use is adequate, with the QIs being able to provide a measurement of the adequacy to the principles of the rational use of antimicrobials agents in a hospital context[8,9].

The implementation of the Antibiotic Stewardship Programs is a trend in several countries[6,22]. Although guidelines assist in the appropriate use of antimicrobial agents, QISs 8-10 have been proposed to assess the adequacy of the use of antimicrobials agents in adult patients. Several QIs have been developed specifically for respiratory tract infection, urinary tract infection and sepsis[23-25]. The evaluation of the quality of the use of antimicrobials agents was carried out according to the study by Van den Bosch *et al* (2015) because, in addition to covering a set of high quality, generic and validated QIs[8], it can be applied to the older adult. In this study, five indicators scored above 50%. Three of the nine QIs significantly influenced the scores of the indicators (QI - 4, QI - 6, QI - 8).

According to the guidelines of the institution's infection control committee, at least two blood samples must be collected, at different sites, in order to identify species of aerobic and anaerobic bacteria in blood culture, before starting systemic antibiotic therapy. A performance lower than 50% in the indicator that measures this recommendation shows the need for actions to make prescribers aware of the importance of the minimum request for two samples for the better identification of the infectious agent, contributing to a more appropriate selection of the antimicrobial agent.

The request of cultures before the prescription of antimicrobial and the empirical prescription according to the institution's guidelines were frequent for the older adult studied. Van den Bosch *et al*. (2016), analyzing the applicability of indicators in hospital practice, points out that a group of patients, depending on clinical specificities, may need an empirical prescription of antimicrobials agents different from the one recommended in the guideline. In the investigated sample, about a quarter of the prescriptions were not in line with the guidelines of the hospital infection commission that guide the empirical use of antimicrobials agents(QI - 3). This finding can be explained by the fact that older adults frequently presents multiple comorbidities and physiological changes that interfere with pharmacotherapy. Therefore, they need greater individualization due to the functionality and clinical condition at the time of empirical selection of the antimicrobial.

The indicator that assesses the need to change from empirical to targeted therapy after the culture results become positive (QI - 4) showed that the change is significant. In general, on the fifth day, culture results are available. Thus, five days after the start of the antimicrobial agent, 97.1% of the prescriptions were changed, guaranteeing the conformity of clinical procedures in relation to institutional guidelines.

Conversion from intravenous to oral therapy usually occurs between two and three days after starting treatment. This can have an impact on reducing the length of hospital stay, greater comfort and safety to the patient, with a reduction in the risk of complications, the incidence of adverse effects related to intravenous therapy, infections related to the use of invasive devices and, finally, it can contribute to the reduction of hospital costs[26]. Early conversion is an important element in antimicrobial agent use management programs[6,22]. To improve adherence to the guidelines described, the recommendations must be developed through the collaboration of the multidisciplinary team, in order to reach a consensus on the approach to be adopted.

The duration of systemic antimicrobial agent therapy and the indication of its beginning in the patient care records are properly developed and the indicators that assess these aspects showed high value demonstrating the adequacy of the guidelines. For patient safety, as well as for infection control actions, it is important to properly record the use of antimicrobial agents, as it contributes to control and monitoring measures.

Therapeutic monitoring is not performed systematically in the hospital where the study was conducted, being at odds with the appropriate use of antimicrobials agents proposed by the indicator. Therefore, it is important to structure guidelines for its performance, considering the risks of adverse events and therapeutic failures due to the lack of dose optimization. Therapeutic drug monitoring was performed in only one patient using vancomycin and in none of the patients treated with aminoglycoside. Regular dosing does not mean constant plasma levels of drugs, especially in the older adult due to differences in the pharmacokinetics of the drug administered. Therefore, it is known that the serum measurement of antimicrobials agents is extremely important for the older adult, as it can assist in the prevention of nephrotoxicity and other adverse events, and in the adequate maintenance of the therapeutic serum concentration[7].

In Brazil, there is a national guideline that orientates the rational use of antimicrobial agents[6,27]. In the investigated hospital, in addition to the definition of criteria for the use of antimicrobials agents defined by the medical auditors of the infection committee, they are structured and published in the form of clinical and therapeutic guidelines. And, although some recommendations of the national guideline are outdated, the information published at the institution is updated and is reassessed every three years. Therefore, we consider that the two quality indicators that describe the recommended care at the hospital level are in line with those suggested by Van den Bosch *et al.* (2015).

Considering the profile of the antimicrobials agents used and the microbial ecology, with the presence of microorganisms that can develop multi-drug resistance, it is essential to evaluate the

implementation of a Antibiotic Stewardship Program, as proposed by the National Directive of the ANVISA (2017) aiming at optimize the use of antimicrobials agents and prevent infections, as well as improve the performance of the indicators used in this investigation.

The main limitation of this study is the retrospective cross-sectional design, related to the information contained in the medical records, such as quality and lack of recorded information, presence of divergences or registration of the patient's actual clinical condition antimicrobial agent use was monitored on a specific day, which may have led to a trend in assessing the average use of anti-infectious drugs. Another limitation is in relation to the QIs proposed by Van den Bosch *et al*. (2015). It was possible to evaluate only eight of the nine items that describe the recommended care at the patient level, because problems related to the unavailability of information in the medical record and filling in the data during hospitalization, such as creatinine dosage and patient weight, made it impossible to evaluate the indicator that analyzes the dose and dosage of the systemic antibiotics in relation to the renal function.

The importance of the role of the pharmaceutical professional with the Hospital Infection Control Commission is highlighted, as it has relevant knowledge about antimicrobial agents, and can also assist in the management of the use of antiseptic, disinfectant and sterilizing agents, which can contribute to the reduced rates of adverse events associated with the use of these drugs.

It is worth mentioning that this study is a pioneer in Brazil and provides the first data on the use of antimicrobials agents in hospitalized older adult. A point prevalence study contributes to assessing the profile of appropriate use of antimicrobial agents, which makes this an important tool for improving the management of antimicrobial agent use in the country.

## Conclusion

The prevalence of antimicrobial agent use in the older adult was high, with a predominance of prescription of penicillins associated with beta-lactamase inhibitors and glycopeptides. Pathogens classified as critical and high priority for the development and research of new treatments were frequent in the hospital, showing the importance of actions to ensure the rational use of antimicrobials agents in the institution. Quality indicators used to evaluate the rational use of antimicrobial demonstrated the need to implement guidelines for therapeutic monitoring of antimicrobials agents in the institution and that empirical therapy is often developed in line with the guidelines recommendations recommended.

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**Collaborators**

LFC, AMMR, CMB participated in the design of the project. LFC participated in data collection and writing of the article. LFC, ACGM, AMMR, CMB participated in the analysis and interpretation of the data; AMMR and CMB performed a critical review of the article. All the authors approved the version to be published and assumed responsibility for all information on the work, ensuring the accuracy and integrity of any part of the work.

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**Conflict of interest statement:**

The authors declare that there are no conflicts of interest regarding this article.

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